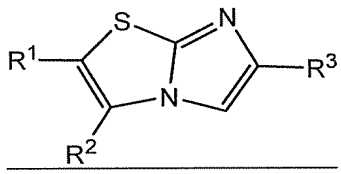
AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method of reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is ~~cleaved~~ cleavable under physiological conditions, whereby the cell protection factor is released from the bone targeting agent in vivo to reduce cell death in bone marrow cells, wherein the cell protection factor is a compound of Formula IV:



(IV)

wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties.

2-6. (Canceled)

7. (Currently Amended) The method of ~~claim 6,~~ claim 1, wherein R^1 and R^2 are taken together to form a 5- or 6-membered aliphatic carbocyclic ring optionally substituted with one or more C_1-C_6 alkyl groups.

8 -16. (Canceled).

17. (Currently Amended) The method of claim 1, wherein the mammal ~~comprises~~ has at least one tumor.

18. (Currently Amended) The method of claim 17, wherein the mammal ~~comprises~~ has at least one $p53^+$ tumor.

19-22. (Canceled)

23. (Original) The method of claim 1, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

24 -26. (Canceled).

27. (Previously Presented) The method of claim 1, wherein the linkage is an acid-cleavable linkage.

28-30. (Canceled).

31. (Previously Presented) The method of claim 27, wherein the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

32-36. (Canceled).

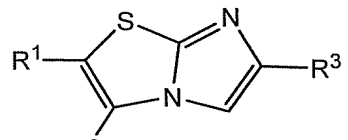
37. (Original) The method of claim 1, wherein the mammal is a human.

38-74. (Canceled).

75. (Previously Presented) The method of claim 7, wherein the cell protection factor is pifithrin-β.

76. (Currently Amended) A method of reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is cleavable under physiological conditions,

wherein the cell protection factor is a compound of Formula IV:



(IV)

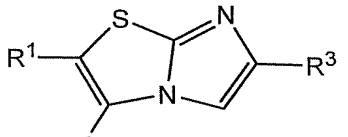
wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties;

whereby the cell protection factor is released from the bone targeting agent *in vivo* to reduce cell death, ~~wherein the cell protection factor is a temporary inhibitor of a tumor suppressor gene~~, the bone targeting agent is a ligand that binds hydroxyapatite, and the linkage is an organic moiety comprising a nucleophilic or electrophilic reacting group which allows covalent linking to the bone targeting agent.

77. (Currently Amended) A method of reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is cleavable under physiological conditions, whereby the cell protection factor is released from the bone targeting agent *in vivo* to reduce cell death, wherein:

wherein the cell protection factor is a compound of Formula IV:



(IV)

wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties;

~~the cell protection factor is a temporary p53 inhibitor;~~

the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide; and

the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

78-80. (Canceled)

81. (Currently Amended) The method of ~~claim 80,~~ claim 76, wherein R^1 and R^2 are taken together to form a 5- or 6-membered aliphatic carbocyclic ring optionally substituted with one or more C_1-C_6 alkyl groups.

82. (Currently Amended) The method of claim [[79]] 1, wherein the cell death reduced is bone marrow cell death.

83-89. (Canceled).

90. (Currently Amended) The method of claim [[79]] 76, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

91. (Canceled)

92. (Currently Amended) The method of claim [[79]] 76, wherein the linkage is an acid-cleavable linkage.

93. (Canceled)

94. (Previously Presented) The method of claim 92, wherein the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

95-99. (Canceled)

100. (Currently Amended) The method of claim [[79]] 76, wherein the mammal is a human.

101-102. (Canceled)

103. (Previously Presented) The method of claim 1, wherein the cell death is reduced by at least 5%.

104. (Currently Amended) The method of claim [[79]] 76, wherein the cell death is reduced by at least 5%.

105. (New) The method of claim 1, wherein R^1 and R^2 together form a 6-membered aliphatic carbocyclic ring and R^3 is phenyl substituted with a C_1-C_6 alkyl group.

106. (New) The method of claim 105, wherein R^3 is phenyl substituted with a methyl group.

107. (New) The method of claim 76, wherein R^1 and R^2 together form a 6-membered aliphatic carbocyclic ring and R^3 is phenyl substituted with a C_1-C_6 alkyl group.

108. (New) The method of claim 107, wherein R^3 is phenyl substituted with a methyl group.

109. (New) The method of claim 77, wherein R^1 and R^2 together form a 6-membered aliphatic carbocyclic ring and R^3 is phenyl substituted with a C_1-C_6 alkyl group.

110. (New) The method of claim 109, wherein R^3 is phenyl substituted with a methyl group.

111. (New) The method of claim 106, wherein the cell protection factor is pifithrin-β.

112. (New) The method of claim 108, wherein the cell protection factor is pifithrin-β.

113. (New) The method of claim 110, wherein the cell protection factor is pifithrin-β.

114. (New) The method of claim 103, wherein the cell death is reduced by at least 10%.

115. (New) The method of claim 104, wherein the cell death is reduced by at least 10%.

116. (New) The method of claim 77, wherein the cell death is reduced by at least 5%.

117. (New) The method of claim 116, wherein the cell death is reduced by at least 10%.

118. (New) The method of claim 76, wherein the mammal has at least one tumor.

119. (New) The method of claim 118, wherein the mammal has at least one $p53^+$ tumor.

120. (New) The method of claim 76, wherein the cell protection factor is pifithrin-β.

121. (New) The method of claim 76, wherein the cell death reduced is bone marrow cell death.

122. (New) The method of claim 77, wherein R^1 and R^2 are taken together to form a 5- or 6-membered aliphatic carbocyclic ring optionally substituted with one or more C_1-C_6 alkyl groups.

123. (New) The method of claim 77, wherein the mammal has at least one tumor.

124. (New) The method of claim 123, wherein the mammal has at least one $p53^+$ tumor.

125. (New) The method of claim 77, wherein the mammal is a human.

126. (New) The method of claim 77, wherein the cell protection factor is pifithrin-β.

127. (New) The method of claim 77, wherein the cell death reduced is bone marrow cell death.